

CLAIMS

What we claim is:

1. A chimeric polypeptide comprising:

- (1) a TNF neutralizer domain;
- (2) an IL-1 receptor antagonist domain; and
- (3) a dimerization domain,

wherein the three domains are operably linked.

2. The chimeric polypeptide of claim 1, wherein the TNF neutralizer domain includes a domain that binds to mammalian TNF or IL-6.

3. The chimeric polypeptide of claim 2, wherein the TNF neutralizer domain includes an extracellular domain of mammalian TNFR or mammalian IL-6 receptor, or its functional equivalent.

4. The chimeric polypeptide of claim 3, wherein the mammalian TNFR is TNFRII or TNFRI.

5. The chimeric polypeptide of claim 3, wherein the mammalian TNFR is human TNFRII.

6. The chimeric polypeptide of claim 1, wherein the IL-1 receptor antagonist domain includes IL-1ra or its functional equivalent.

7. The chimeric polypeptide of claim 6, wherein the IL-1ra is a glycosylated mammalian polypeptide.

8. The chimeric polypeptide of claim 1, wherein the dimerization domain includes a human Ig Fc fragment.

9. The chimeric polypeptide of claim 8, wherein the human Ig Fc fragment is an IgG1 Fc fragment.
10. The chimeric polypeptide of claim 1, wherein the chimeric polypeptide includes, from the N-terminus to the C-terminus, a TNF neutralizer domain, a dimerization domain, and an IL-1 receptor antagonist domain; or functional equivalents thereof.
11. The chimeric polypeptide of claim 10, wherein the chimeric polypeptide includes an extracellular domain of human TNFRII, human IgG1 Fc, and IL-1ra; or functional equivalents thereof.
12. The chimeric polypeptide of claim 11, wherein the chimeric polypeptide includes SEQ ID NO:2.
13. A polynucleotide comprising a sequence encoding the chimeric polypeptide of claim 1.
14. A cell comprising a polynucleotide of claim 13.
15. The cell of claim 14, wherein the cell is a mammalian cell, a bacterial cell, a yeast cell, an insect cell, or a plant cell.
16. The cell of claim 15, wherein the cell is a CHO cell or a NSO cell or a SP/2/0 cell.
17. A composition comprising a chimeric polypeptide of claim 1 and a pharmaceutical acceptable carrier.
18. A composition comprising a polynucleotide of claim 13 and a pharmaceutical acceptable carrier.

19. A method of treating a TNF and IL-1 dependent disorder, comprising administering to a subject in need thereof an effective amount of a composition of claim 17.
20. The method of claim 19, wherein the disorder is an inflammatory disorder.
21. The method of claim 20, wherein the inflammatory disorder is rheumatoid arthritis or psoriasis.
22. A method of treating a TNF and IL-1 dependent disorder, comprising administering to a subject in need thereof an effective amount of a composition of claim 18.
23. The method of claim 22, wherein the disorder is an inflammatory disorder.
24. The method of claim 23, wherein the inflammatory disorder is rheumatoid arthritis or psoriasis.
25. A vector comprising a polynucleotide of claim 13.
26. A method of producing a polypeptide, comprising culturing the cell of claim 14 in a medium under conditions permitting expression of a polypeptide encoded by the polynucleotide, and purifying the polypeptide from the cultured cell or the medium of the cell.